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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,836	06/01/2001	Shikha P. Barman	08191-018001	3677

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/872,836	BARMAN ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,21-29,31-34 and 37* is/are pending in the application.

4a) Of the above claim(s) *5 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-16, 21-24, 26-29, 31-34 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 26, 2007 that includes a response to the final office action dated July 26, 2006, has been entered. No claims were amended, canceled or newly added. Claims 1-16, 21-29, 31-34, and 37 are currently pending in the application. Claims 5 and 25 remain withdrawn from consideration, without traverse. Claims 1-4, 6-16, 21-24, 26-29, 31-34 and 37 are under current examination.

Non-compliance with 37 CFR 1.121

The amendment to the claims submitted December 21, 2006 fails to comply with 37 CFR 1.121(c), as claims 5 and 25 contain incorrect status identifiers. Claims 5 and 25 were withdrawn from consideration in the office action dated 1/25/2005. While the amendment has been entered, please note that compliance with 37 CFR 1.121 is required for all future claim amendments. Failure to comply may result in non-entry of the amendment.

Response to Claim Rejections – 35 USC § 102(e)

Claims 1-4, 6-7, 9-16, 29, and 37 were rejected under 35 USC 102(e) as being anticipated by Papahasdjopoulos *et al.* (U.S. Patent No.: 6,803,053; of record), in the previous action dated 10/6/2005.

In view of Applicants' arguments and upon further consideration of the claim limitation "a polymeric matrix", the rejection is hereby withdrawn. To the extent that Applicants' arguments may apply to other rejections, such arguments are addressed below.

Response to Claim Rejections – 35 USC § 103(a)

Claims 21-24, 27, and 31 were rejected under 35 USC 103(a) as being unpatentable over Papahasdjopoulos *et al.* (U.S. Pat No. 6,803,053; of record), taken with Carson (U.S. Patent Publication No.: 2003/0109469; of record), as evidenced by Adema (U.S. Patent No.: 6,500,919; of record); and claims 21-24, 27, 28, and 31 are rejected under 35 USC 103(a) as being unpatentable over Papahasdjopoulos *et al.* taken with Rolland (U.S. Patent No.: 6,040,295; of record), and Lunsford (U.S. Patent Publication No.: 2002/0182258; of record)., and further in view of Carson, as evidenced by Adema. in the previous action dated 10/6/2005. In view of Applicants' arguments and upon further consideration of the claim limitation "a polymeric matrix", the rejections are hereby withdrawn. The claims are however subject to new rejections as detailed below.

Claims 1-4, 6-16, 29, 32-34, and 37, stand rejected under 35 U.S.C. 103(a) as being unpatentable over Papahasdjopoulos *et al.* taken with Rolland (U.S. Patent No.: 6,040,295; of record), and further in view of Lunsford (U.S. Patent Publication No.: 2002/0182258; of record).

Claims 1-4, 6, 7, 9-16, 26, 29, 32-34, and 37, stand rejected under 35 U.S.C. 103(a) as being unpatentable over Papahasdjopoulos *et al.* taken with Rolland, and further in view of Mathiowitz (U.S. Patent No.: 6,677,313; of record). The rejections set forth pp. 5-10 of the office action dated October 6, 2005 are maintained for claims 1-4, 6-16, 26, 29, 32-34, and 37 for reasons of record.

Applicants traverse the rejection and argue that entrapment of a targeting moiety-containing complex disclosed by Papahadjopoulos within a composition of Lunsford or Mathiowitz would have been expected to partially or completely mask the targeting moieties of Papahadjopoulos and thereby reduce or eliminate their targeting function. Thus, the person of ordinary skill in the art would have lacked the requisite suggestion or motivation entrap a complex of Papahadjopoulos within a composition of Lunsford or Mathiowitz.

Applicants' arguments have been fully considered, but are not found to be persuasive. The previous office action set forth the following: "it would have been obvious for one of ordinary skill in art to employ known polymeric microparticles such as those disclosed in Lunsford to entrap and enhance the stability of the lipid:nucleic acid:PEG-DSPE complexes of Papahasdjopoulos et al." The preceding statement does not recite any language regarding

targeting-moiety containing complexes, therefore such a modification was not proposed in this instance. The inclusion of PEG-DSPE in the complex of Lunsford is commensurate in scope with that of instant claims 1 and 37.

Further, in response to applicant's argument regarding the entrapment of a targeting-moiety containing complex disclosed by Papahadjopoulos within the composition of Lunsford or Mathiowitz, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Moreover, there is no teaching in Lunsford that their polymers would have eliminated the targeting function of the targeting moieties. Papahadjopoulos describes a microparticle characterized by targeting moieties attached thereto, for the delivery of lipid/nucleic acid complexes to a desired target. In column 2, lines 44-56, Rolland also describes the use of targeting ligands for the enhanced translocation of nucleic acids to specific tissues or cells. Lunsford claims (section 21, claim 1), a microparticle comprising a polymeric matrix, a lipid and a nucleic acid molecule that is not encapsulated. Neither Papahadjopoulos, nor Lunsford require the encapsulation method described by Mathiowitz. The reference to Mathiowitz was used for an entirely different purpose and to address a separate limitation. Mathiowitz was not used to require the products of Papahadjopoulos, or Lunsford be encapsulated. Finally, in column 10, lines 44-45, Papahdjopoulos specifically states, "if the particle is a vesicle, the linker/protein molecules will only be present on the outer surface". Therefore Applicant's assertion that the targeting moieties would have been expected to be partially or completely masked is not supported. As stated in MPEP 2145, I. The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) <http://www.uspto.gov/web/offices/pac/mpep/documents/0700_716_01_c.htm> for examples of attorney statements which are not evidence and which must be supported by an appropriate

affidavit or declaration. Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c).

With respect to the recited limitation of a lipid having a pKa of less than about 2.5, while neither the instant specification, nor the art of record discloses a pKa value for the elected species of PEG-DSPE, the pKa value is an inherent property of the lipid. As such, said limitation is inherently possessed by the elected lipid PEG-DSPE and is immaterial to the patentability of the claimed invention. The PEG-DSPE taught by Papahdjopoulos cannot have a pKa value that is different from the PEG-DSPE lipid of the instant invention. As stated in MPEP 2112: The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." In re Napier, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir.1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also In re Grasselli, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).

Moreover, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Therefore, the rejection of claims 1-4, 6-16, 26, 29, 32-34, and 37 is maintained for reasons of record and the foregoing discussion.

New Claim Rejections – 35 USC § 103(a)

Claims 21-24, 26-28, and 31 are newly rejected under 35 USC 103(a) as being unpatentable over Lunsford (U.S. Patent Publication No.: 2002/0182258; of record, in view of Papahasdjopoulos *et al.* (U.S. Pat No. 6,803,053; of record).

The claims embrace a lipidic microparticle less than 100 microns or less than 50 microns, or lipidic microparticles comprising a PEG-DSPE (a lipid phosphonate) and a polymeric matrix, wherein the microparticle is not encapsulated in a liposome, a nucleic acid molecule encoding a peptide having a length and sequence that permit it to bind to an MHC class I molecule, and a method of administering said microparticle to an animal.

Lunsford et al. disclose a preparation of microparticles for delivery of nucleic acids comprising a polymeric matrix, a nucleic acid expression vector, and a lipid, wherein the microparticles have a diameter less than about 100 microns (Abstract and Title). The microparticle may be less than 20 microns (claim 1), and the nucleic acid of the microparticle may comprise an expression control sequence operatively linked to a coding sequence (claim 4) that is a peptide having a length and sequence which permit it to bind to an MHC class I molecule (claim 8(c)). The encoded polypeptide may consist of at least two peptides linked in tandem, wherein the at least two peptides are not identical (claim 14), or are overlapping (claim 15), or are immunogenic (claim 18). The microparticles are further disclosed in a method of administering nucleic acid to an animal (claim 51).

While Lunsford et al. do not specifically disclose the lipid of the microparticle as PEG-DSPE, they state that the lipid may be a cationic lipid (claim 9) or a phospholipid (claim 11), thus providing the motivation to incorporate any cationic lipid or phospholipids in their polymeric matrix to form a microparticle.

Papahasdjopoulos *et al.* disclose lipidic microparticles linked to targeting moieties (Abstract), prepared by contacting a nucleic acid with an organic polycation and an amphiphilic cationic lipid and then combining the complex thus formed with a hydrophilic polymer, that may be PEG-DSPE (columns 3 and 4 bridging). Papahasdjopoulos et al. clearly teach that "the lipids need not be provided as a liposome." (column 10). They further state: "It is also recognized that after complexation, the lipid:nucleic acid complex may no longer exist as a true vesicle and therefore is not generally regarded as a liposome." (column 10). As such, the microparticles of Papahasdjopoulos *et al.* are not encapsulated in a liposome and do not comprise a cell. With respect to the recited limitation of lipid pKa, the pKa associated with PEG-DSPE is a property inherently possessed by the lipid and is immaterial to the patentability of the claimed invention.

Thus, at the time of the instant invention it would have been *prima facie* obvious for one of ordinary skill in the art to include PEG-DSPE disclosed by Papahasdjopoulos *et al.* in the microparticle of Lunsford et al., with a reasonable expectation of success, to produce the microparticle of the instantly claimed invention. One of ordinary skill in the art would have been motivated to utilize PEG-DSPE as a lipid in the polymeric matrix composition of Lunsford et al., because the inclusion of cationic and phospholipids was expressly provided for by Lunsford et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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Examiner, AU 1633

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